Number/Name: P-18-0068 / [redacted]

UPDATED 2/21/18 based on new information from submitter on the worker inhalation exposures

Updated with Worker inhalation estimates of the submitter on Aug 2nd, 2018 (P180068.en5)

UPDATED 8/8/18 based on new information with updated assessment based on the Post-Focus Draft Revision 4 dated 5/30/2018.

SUMMARY INFORMATION

EPA estimated the human health hazard of this chemical substance based on its estimated physical/chemical properties and by comparing it to structurally analogous chemical substances for which there is information on human health hazard.

Based on the hazard determination and available quantitative and/or qualitative risk information, EPA concludes that there is risk for the PMN substance **.**

Human Health Hazard:

- Expect poor absorption via all routes (pchem).
- Concerns for lung overload
- Concern for irritation to eyes, skin, lungs based on the SDS.
- PMN will slowly react to [redacted]
    - Unlikely to have inhalation exposures to [redacted] in an occupational setting unless alkaline or acid conditions are present.
    - To the extent [redacted] are bioavailable:
        - Concern for skin sensitization in humans
        - Concern for systemic effects based on analogy to [redacted] with increased cholesterol, although the database is highly uncertain.

Human Health Risk:

- Risks were identified for workers for lung overload via the inhalation exposures of respirable and total particles based on quantitative hazard data for [redacted] an analogue ($MOE_{respirable}$= 70 ; MOE_{total}=23.1; benchmark = 100, and inhalation fold factor of 1.4 and 4.2). Risks can be mitigated if exposures can be controlled by the use of appropriate, effective PPE including a respirator with an APF of 10.
- Eye, skin and lung irritation hazards to workers were identified based on the SDS. Risks were not quantified due to a lack of dose-response data for these hazard. Risks would be mitigated if exposures can be controlled by the use of eye protection, impervious gloves and respiratory protection (an APF cannot be quantified).
- Risks were not identified for workers for sensitization via inhalation and dermal contact because the [redacted] is not expected to be bioavailable in an occupational setting.
- Risks were not identified for general population for lung over load as exposures were below modeling thresholds.

- Risks were not identified for general population for sensitization via drinking water and fish ingestion due to [redacted] Although the [redacted] could be bioavailable via ingestion, risks were not considered likely via this route based on the expected dilution in the media.
- Risks to consumers were not evaluated because consumer uses were not identified as conditions of use
- .

Assumptions and Uncertainties

- Absorption of the PMN is based on p-chem properties.
- The rate of transformation to [redacted] is uncertain and the extent [redacted] bioavailablility is uncertain.
- Inhalation exposures to [redacted] are unlikely in an occupational setting unless alkaline or acid conditions are present.
- The
- The database is highly uncertain for the systemic effects which are based on analogy to [redacted]
- Releases of stack and fugitive aire were below threshold, therefore risks to general population via inhalation route and for consumers via all routes of exposures were not quantified.

Potentially Useful Information

- Potentially useful information would inform understanding of absorption, skin irritation, eye damage, specific target organ toxicity or pulmonary effects.

PART A

SAT Date: 12/22/2017

SAT Chair: William Irwin

Health Assessor: Chris Brinkerhoff

QC Reviewer: Tracy Behrsing 12/27/2017

Structure:

PMN: P-18-0068	Submit [redacted]			Manu.	Import
Max. PV (KG): [redacted]		Binding Option Marked:		X	
MW: [redacted]	% < 500	[redacted]	% <1000	CASNO.: None	
PMN Structure		Prop.	Meas.	Est.	
[redacted]		MP			
		BP			
		Pres.		at 760 mm Hg	
		VP		<0.000001	
		S-H2O		<0.000001/Rea	
		log P			
Chemical Name		Analogs:			
[redacted]		[redacted]			
[redacted]		other uses			
		[redacted]			

- **CASRN:** none
- **Chemical Category:** lung overload / respirable, poorly soluble particulates category
- **Chemical Category Health Concerns:**

For Lung overload:

The category concerns discussed here are <u>limited to effects on the lung</u> as a result of inhaling the particles. Broadly, as shown in rat inhalation studies (e.g., for polymers, Muhle et al., 1990a, 1990b, 1991; Bellmann et al., 1991, 1992), these effects range from

inflammation to fibrosis to, potentially, cancer (demonstrated for some poorly soluble inorganic particulates, but not specifically for poorly soluble polymers). Because it is not known with certainty whether high lung burdens of poorly soluble polymers can lead to lung cancer in humans via mechanisms similar to those for poorly soluble inorganic particulates in the rat, in the absence of mechanistic data to the contrary, it must be assumed that the rat model can identify potential carcinogenic hazards to humans. Since the apparent responsiveness of the rat model at overload is dependent on coexistent chronic active inflammation and cell proliferation, at lower lung doses in which chronic active inflammation and cell proliferation are not present, no lung cancer hazard is anticipated based on that mode of action (ILSI, 2000).

- **Category Testing Strategy:**
  - Tiered tests for insoluble polymer lung overload
- **SAT Key Words:**
  - Lung, Irritation- Eye, Skin. Lung
- **Absorption:**
  - Expect poor absorption via all routes (pchem).
- **SAT Health Summary:**
  Concerns for lung overload. SDS: concern for irritation to eyes, skin, lungs. Based on discussions at SAT, there is unlikely inhalation exposure to [redacted] in an occupational setting unless alkaline or acids conditions are present. To the extent [redacted] is bioavailable, some [redacted] compounds have caused skin sensitization in humans with [redacted] having oral LD50 values over 1688 mg/kg (Ullmann's Ulmman's Encylopedia for Industrial Chemicals).

- **PMN Data:** (study summary, POD)
  - None submitted
- **Analog Data:** (analog, structure, study summary, POD)
  - For [redacted], the LOAEL in a rat chronic study was 0.79 mg/kg/day based on increased cholesterol (PPRTV, 2012).
    - High uncertainy associated with this study. Not considered adequate to derive a provisional toxicity value (PPRTV) based on a single dose study and the study had an epidemic of virulent pneumonia in the rat colony which killed a number of animals. [redacted]
- **Other Information:** (structural alert or component of interest, basis, etc.)
  - SDS

2.2 Potential Health Effects

Carcinogenicity Information: Constituents are not classified as a carcinogen by IARC, OSHA, NTP or EPA.
Skin Exposure: May cause irritation with prolonged or repeated skin exposure
Eye Exposure: Contact with eyes may cause irritation.
Inhalation: May cause irritation to the respiratory tract.
Swallowing: May be harmful if swallowed

- **Point of Departure Selected and Basis:**
  For ingestion only: expect release of [redacted] – recommend use of the [redacted] LOAEL of [redacted] mg/kg/day as long as consideration for the many uncertainties in that result is included. (As noted in the ISIS file for this PMN, the [redacted] (Note – given the database uncertainty, this was not used to quantify risks. CBA 1/8/18)

POD for lung overload to insoluble particles

POD type: NOAEC
POD Value: 4 mg/m^3
POD Chemical: [redacted]
POD Route: Inhalation
POD Hazard Endpoint: Lung overload
POD Basis: Rats were exposed by inhalation to 0 (air controls), 1, 4, or 16 mg/m3 of the PMN substance 6 hr/day, 5 days/wk for 90 days. At the highest concentration, rats developed inflammation of the lung and larynx. Similar results were seen in the 14-day range-finding study at concentrations ranging from 10 to 100 mg/m3. The NOAEL from this study is 4 mg/m3. The NCEL for analogous particulates would be 0.04 mg/m3.
POD Benchmark MOE: 100
[redacted]

On further consideration of this PMN case and after deliberations with the chemists, it was decided that this PMN fits the "Respirable, Poorly Soluble Particulate" category in the 2010 chemical category document, there are several PODs available to quanify the lung over load and we choose to quantifiy the risk with anologue [redacted] which would be closer to thePMN than the previously suggested insoluble poly vinyl chloride.

Exposure Routes of Interest:

- _X_Inhalation
- _X_Dermal
- _X_Ingestion

PART B

Focus Date: 01-04-2018

Focus Assessor: Sailesh Surapureddi

QC: Baier-Anderson

Updated with Worker inhalation estimates of the submitter on 8/2/18 (P180068.en5)

Updated with Gen Pop exposures on 8/8/18 (updated assessment based on the Post-Focus Draft Revision 4 dated 5/30/2018.)

USES and EXPOSURES:

- **Uses:** [redacted]
- **Worker Exposure:**
  - **Inhalation:**
    - **Processing:** [redacted]
      - Exposure to [redacted] (Class I)-
        - **OSHA PEL =** [redacted] **mg/m -respirable**
          - Potential Dose Rate: [redacted] **mg/day** over [redacted] days/yr
        - **OSHA PEL =** [redacted] **mg/m^3 (total)**
          - Potential Dose Rate: Inhalation Particulate [redacted] **mg/day** over [redacted] days/year- Basis: [redacted]
    - **Use:** [redacted]
      - Exposure to [redacted] (Class I)-
        - **OSHA PEL =** [redacted] **mg/m -respirable**
          - Potential Dose Rate: [redacted] **mg/day** over [redacted] days/yr
        - **OSHA PEL =** [redacted] **mg/m^3 (total)**
          - Potential Dose Rate: Inhalation Particulate [redacted] **mg/day** over [redacted] days/year- Basis: [redacted]
      - Exposure to [redacted] (Class I)-
        - **OSHA PEL =** [redacted] **mg/m -respirable**
          - Potential Dose Rate: [redacted] **mg/day** over [redacted] days/yr
        - **OSHA PEL =** [redacted] **mg/m^3 (total)**
          - Potential Dose Rate: Inhalation Particulate [redacted] **mg/day** over [redacted] days/year- Basis: [redacted]
      - Exposure to [redacted] (Class I)-
        - **OSHA PEL =** [redacted] **mg/m -respirable**
          - Potential Dose Rate: [redacted] **mg/day** over [redacted] days/yr
        - **OSHA PEL =** [redacted] **mg/m^3 (total)**
          - Potential Dose Rate: Inhalation Particulate [redacted] **mg/day** over [redacted] days/year- Basis: [redacted]
  - **Dermal:**
    - Exposure to [redacted] at [redacted] concentration
      - Potential Dose Rate: [redacted] **mg/day** over [redacted] day/year- Basis: [redacted]

- Exposure to [redacted] at [redacted] concentration
  - Potential Dose Rate: [redacted] mg/day over [redacted] day/year- Basis: [redacted]
- Exposure to [redacted] at [redacted] concentration
  - Potential Dose Rate: [redacted] mg/day over [redacted] days/yr- Basis: [redacted]

- **General Population Exposure:**
  - **Drinking Water: ADR as high as 2.3E-6 mg/kg/day**
  - **Fish:** ADR as high as **7.27E-6 mg/kg/day**
  - **Air/Inhalation:** below modeling thresholds

This updated assessment is based on the Post-Focus Draft Revision 4 dated 5/30/2018.

Exposure Scenario	Water						Land fill(non-sludge)	Stack		Fugitive	
Release Activity(ies) exposure Calculations	Drinking Water		Fish Ingestion		7Q10cc 1000 ug/l	PDM Exceeded # Days	LADD mg/kg/day	ADR mg/kg/day	LADD mg/kg/day	ADR mg/kg/day	LADD mg/kg/day
	ADR mg/kg/day	LADD mg/kg/day	ADR mg/kg/day	LADD mg/kg/day							
M+P+U:Max ADR	2.35e-6	--	7.27e-6	--	--	--	--	-- (--)	-- (--)	-- (--)	-- (--)
M+P+U:Max LADD	--	1.14e-9	--	8.23e-10	--	--	--	-- (--)	-- (--)	-- (--)	-- (--)

- **Consumer Exposure: not expected**

RISK CALCULATIONS:

- **Worker Calculations:**
  - Risks were identified for workers for lung overload via the inhalation exposures of respirable and total particles based on quantitative hazard data for Lithium Manganese Oxide an analogue ($MOE_{respirable}$= 70 ; MOE_{total}=23.1, benchmark = 100, and inhalation fold factor of 1.4 and 4.2).

Lung Overload: Respirable, Poorly Soluble Particles : POD = 4.0 mg/m^3, Benchmark MOE = 100

Worker Margin of Exposure (MOE) Calculations using Animal Oral POD and Engineering Report PDR

	Animal or Human POD			Worker Exposure				Human Breathing Rates						Benchmark MOE	Endpoint Type
Exposure Route	POD Conc. mg/m^3	POD Period hrs/day	POD Duration days/wk	Exposure mg/day Potential Dose Rate (PDR)	Total Worker Breathing Volume for PDR Exposure Period m^3	Worker Exposure Duration Hours/Day	Exposure Duration Days/Wk	Default	Worker	Structural Alert as % of PMN	POD Conc - Duration & Breathing Rate Correction Scenario$_{HEC}$ mg/m^3	Exposure TWA mg/m^3	**Margin of Exposure MOE**	100	NOAEL
Inhalation-Respirable	4.0E+00	6.00	5	2.1E-01	10.0	8.00	5	4.90	10.00	100%	1.5E+00	2.1E-02	**70.00**	Fold Factor =	1.4
Inhalation-Total	4.0E+00	6.00	5	6.2E-01	10.0	8.00	5	4.90	10 00	100%	1.5E+00	6.2E-02	**23.71**	Fold Factor =	4.2

- **General Population Calculations:**
  - Risks were not identified for General population for lung over load as the exposure values were below modeling threshold.
  - Risks were not identified for general population for sensitization or irritation via drinking water and fish ingestion due to [redacted] Although the [redacted] could be bioavailable via ingestion, risks were not considered likely via this route based on the expected dilution in the media.

  - **Consumer Calculations:**
  - Risks to consumers were not evaluated as consumer uses were not identified as conditions of use.